III. Remarks

Summarizing the Office Action, all of the pending claims have been rejected. Claims 15-23 and 26 were withdrawn from consideration.

Claim Rejections - 35 USC § 112, first and second paragraphs

Claims 1-14, 24-25 and 27-33 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement in that the specification fails to provide support that any or all known "optically active acids" are applicable in the instant process.

Claims 1-14, 24-25 and 27-33 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement in that the term R' in claim 1, line 6, is not defined in the specification so as to determine the structures of compounds that are included and/or excluded by the term since the term is defined with the phraseology "such as" on line 15, page 5 of the specification and the listed compounds are deemed examples only.

The examiner acknowledges that by amending the claims to recite the specific optically active acids and compounds represented by R' having support in the specification, the rejection would be overcome.

Applicant has amended claim 25 to recite the optically active acids references disclosed in the specification at page 12, lines 12-18, thus obviating this ground for rejection.

Applicants disagree with the Examiner's requirement for "literal support" for the claimed invention, rather than the appropriate standard of conveying to one having ordinary skill in the art that the applicant had possession of the concept of what was claimed. Applicant believes that the Examiner has not established a *prima facie* case of indefiniteness. For example, the Court has

ruled that the term "aryl and substituted aryl radicals", which is a broad term, is not objectionable for this reason alone if the term is supported by the specification, and if it properly defines the novel subject matter described in the specification. The court further stated "It is not contemplated by the public purpose of the patent laws nor required by the statute that an inventor shall be forced to accept claims narrower than his invention in order to secure allowance of his patent." *In re* Sus, 306 F.2d 494, 134 USPQ 301, 304 (C.C.P.A. 1962). Conversely, however, the court has ruled that the term "mineral carbon" was indefinite for lack of adequate definition in the specification. *Ex parte* Saceman, 27 USPQ2d 1472 (B.P.A.I. 1993).

Applicant strongly urges the view that this functional definition is all that is necessary for one skilled in the art and that applicant's further disclosure, immediately following this functional definition, of exemplification of certain compounds meeting this functional requirement, is non-essennal and provides additional guidance only as to preferred useful compounds.

However, in an effort to move the prosecution of this case to allowance, Applicant has amended claim 1 to recite the specific compounds represented by R'. Support for this Amendment is found in the specification at page 5, lines 15-20 and at claim 2 which has been deleted via this amendment.

The examiner states that, as now amended, claims 1-14, 24-25, and 27-33 lack support in the specification because, according to the specification, page 3, hydroxylamine is reacted formula I in step (a) while 4 fluorophenylmagnesium is reacted with formula III in step (b), and step (c) requires reacting 3-(dimethylamino)propyl magnesium halide with formula (IV) in order to obtain formula (V). However, since when R is H, that is, no substitution, step (e) should be optional because it is not required.

Under the 35 U.S.C. §112, second paragraph rejection, the Examiner is alleging that the claims do not set forth the subject matter that an applicant regards as the invention, and do not particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent. The Examiner is basing the §112, second paragraph rejection on the written description. That is, the scope of the claims is not clear to a hypothetical person possessing an ordinary level of skill in the pertinent art.

Applicant has amended claim 1 to correct the claim in accordance with the specification. No new matter is added via this amendment. This amendment obviates this ground for rejection

Claim Rejections - 35 USC § 103

Claims 1-14, 24-25, and 27-33 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Guazzi et al., WO 02/48133.

Applicant claims a process of making citalopram from 5-formylphthalide as set forth in steps (a) to (f) in claim 1. In an optional embodiment the H of OH in hydrozylamine (a reagent) can be replaced with any substituent, which is inert under Grignard reaction condition. Applicant also claims enantiomeric separation of formula V or VI with tartaric acid or camphosulfonic acid.

The examiner states that Guazzi et al. teach a similar process of making citalopram (formula I) from 5- formylphthalide and that the substituents R' are taught by Guazzi et al., on page 5, last line to page 6, line 4. the examiner also states that all the reagents in the instant steps are the same as that of Guazzi et al. Therefore, the examiner concludes that the instant process is no more than a selective combination of the process of Guazzi et al., done in a manner obvious to one of ordinary skill in the art.

Applicant respectfully disagrees and traverses this rejection.

The present invention is directed to a simple route to synthesize citalopram from 5-formylphthalide, through the preparation of an inert, under conditions of a Grignard reaction, o-substituted oxime which when submitted to two Grignard reactions in sequence and to cyclization, affords an o-substituted 1-[3-(dimethylamino)propyl]-1(4-fluorophenyl)-1,3-dihydro-5-isobenzofurancarbaldoxime which can easily give citalopram.

Unlike the present invention, the starting material of Guazzi is an acetal. The starting material of the present invention is Compound VIII of Guazzi. The starting material of the present invention is reacted with hydroxylamine to produce an o-substituted oxime. In Guazzi an oxime is not produced until the next to last step of the process. Moreover, Guazzi does not protect the oxime but rather compound VIII. Contrary to the examiner's argument, the substituents R' are not taught on page 5, last line to page 6, line 4 since Guazzi does not disclose or even remotely suggest the possibility of protecting the oxime. Moreover, because of the acetal starting material, the Guazzi process requires transformation of the 5-oxime via formation of an acetyloxime followed by acetic acid elimination at high temperature. That is, the acetal must be removed by acid hydrolysis. Unlike Guazzi, the reaction of hydroxylamine and the starting ketone in the present invention yields an oxime.

Guazzi modifies the starting material in a series of process steps to form the compounds of formulas (VII), (VI), and (V), none of which are formed in the applicant's process. The present invention reacts the starting material to form an oxime of formula (III) which is not formed in Guazzi's process. Thus, multiple process steps are different.

Therefore, since the prior art does not provide any indication that such an improvement would have been achieved by modifying the process of Guazzi, as done by the present invention,

it is respectfully suggested that the Guazzi reference does not establish a *prima facie* case of obviousness.

Any fee due with this paper may be charged on Deposit Account 50-1290.

Respectfully submitted,

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